#### **CLAIMS**

#### 1. A compound of formula I

$$R^{5}$$
 $R^{5}$ 
 $R^{5}$ 
 $R^{4}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 

in free or salt form, wherein

R<sup>2</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>5</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by pyridyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is fluoro or C<sub>1</sub>-C<sub>8</sub>-haloalkyl,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by hydroxy or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>8</sub>-haloalkyl,

or Ra is hydrogen or C1-C4-alkyl, Rb is C1-C8-alkyl substituted by nitrile, R3 is fluoro, and R4 is R7,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by hydroxy,  $R^3$  is fluoro, and  $R^4$  is  $R^7$ ,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by di( $C_1$ - $C_8$ -alkyl)amino,  $R^3$  is  $R^6$ , and  $R^4$  is  $C_1$ - $C_8$ -haloalkyl,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by -O- $C_1$ - $C_8$ -alkyl-OH,  $R^3$  is  $R^6$ , and  $R^4$  is fluoro or  $C_1$ - $C_8$ -haloalkyl,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is -CH(CH<sub>3</sub>)-CH<sub>2</sub>-OH, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is fluoro,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by pyrrolidinyl substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $C_1$ - $C_8$ -haloalkyl,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by oxazolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is nitrile or imidazolyl,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by imidazolyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is fluoro,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by benzoimidazolyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is fluoro,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by isoxazolyl substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by pyrrolyl substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by pyrazolyl substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by -CO-O-CH<sub>3</sub>, -CO-O-butyl, -CO-di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino, -CO-NH<sub>2</sub>, -NH-CO-C<sub>1</sub>-C<sub>8</sub>-alkyl, -SO<sub>2</sub>-C<sub>1</sub>-C<sub>8</sub>-alkyl, -CO-NH-R<sup>c</sup> where R<sup>c</sup> is napthyl, or by -CO-NH-C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by di(C<sub>1</sub>-C<sub>8</sub>-alkyl)-amino, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is -CH(CH<sub>3</sub>)-CO-NH-C<sub>1</sub>-C<sub>8</sub>-alkyl or -CH(CH<sub>3</sub>)-CO-O-C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by -CH(OH)-CH<sub>2</sub>-OH, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by  $C_1$ - $C_8$ -alkoxy, or by -S- $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being substituted by oxo, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by a 5- or 6-membered heterocyclic ring having three or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl,

-C1-C8-alkyl-di(C1-C8-alkyl)amino, or by C3-C8-cycloalkyl, R3 is R6, and R4 is R7,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by oxazolyl substituted by  $C_3$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by imidazolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by hydroxy or C<sub>1</sub>-C<sub>8</sub>-alkoxy, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by -CO-Het where Het is a 5- or 6-membered heterocyclic ring having two or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>b</sup> is a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being substituted by oxo, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or  $R^a$  is hydrogen or  $C_1$ - $C_4$ -alkyl,  $R^b$  is an aza-bicyclo[3.2.1]oct-3-yl ring optionally substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> and R<sup>b</sup> together form an azetidine ring substituted by C<sub>1</sub>-C<sub>8</sub>-alkoxycarbonyl or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> and R<sup>b</sup> together form a pyrrolidine ring substituted by -CO-NH<sub>2</sub> or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> and R<sup>b</sup> together form an imidazo-pyridine ring, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>;

R<sup>2</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl or halogen;

R<sup>5</sup> is hydrogen, halogen or C<sub>1</sub>-C<sub>8</sub>-alkyl;

R<sup>6</sup> is halo, -SO<sub>2</sub>-CH<sub>3</sub>, -SO<sub>2</sub>-CF<sub>3</sub>, carboxy, -CO-NH<sub>2</sub>, -CO-di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino, or a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by halo, cyano, oxo, hydroxy, carboxy, nitro, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl, C<sub>1</sub>-C<sub>8</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>8</sub>-alkoxy

optionally substituted by aminocarbonyl, or C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by hydroxy, C<sub>1</sub>-C<sub>8</sub>-alkoxy, C<sub>1</sub>-C<sub>8</sub>-alkylamino or di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino;

 $R^7$  is hydrogen, halo, -SO<sub>2</sub>-CH<sub>3</sub>, nitrile, C<sub>1</sub>-C<sub>8</sub>-haloalkyl, imidazolyl, C<sub>1</sub>-C<sub>8</sub>-alkyl, -NR<sup>8</sup>R<sup>9</sup>, or -SO<sub>2</sub>-NR<sup>8</sup>R<sup>9</sup>; and

R<sup>8</sup> and R<sup>9</sup> are independently hydrogen, amino, C<sub>1</sub>-C<sub>8</sub>-alkylamino, di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino, or C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by hydroxy,

or R<sup>8</sup> and R<sup>9</sup> together form a 5- to 10-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by halo, cyano, oxo, hydroxy, carboxy, nitro, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl, C<sub>1</sub>-C<sub>8</sub>-alkylcarbonyl, C<sub>1</sub>-C<sub>8</sub>-alkoxy optionally substituted by aminocarbonyl, or C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by hydroxy, C<sub>1</sub>-C<sub>8</sub>-alkoxy, C<sub>1</sub>-C<sub>8</sub>-alkylamino or di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino.

## 2. A compound according to claim 1, wherein

Ra is hydrogen, Rb is C1-C8-alkyl substituted by pyridyl, R3 is R6, and R4 is fluoro or C1-C8-haloalkyl,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by hydroxy or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>8</sub>-haloalkyl,

or Ra is hydrogen, Rb is C1-C8-alkyl substituted by nitrile, R3 is fluoro, and R4 is R7,

or Ra is hydrogen, Rb is C1-C8-alkyl substituted by hydroxy, R3 is fluoro, and R4 is R7,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by di( $C_1$ - $C_8$ -alkyl)amino,  $R^3$  is  $R^6$ , and  $R^4$  is  $C_1$ - $C_8$ -haloalkyl,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by -O- $C_1$ - $C_8$ -alkyl-OH ,  $R^3$  is  $R^6$ , and  $R^4$  is fluoro or  $C_1$ - $C_8$ -haloalkyl,

or Ra is hydrogen, Rb is -CH(CH3)-CH2-OH, R3 is R6, and R4 is fluoro,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by pyrrolidinyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is C<sub>1</sub>-C<sub>8</sub>-haloalkyl,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_8$ -alkyl substituted by oxazolyl substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is nitrile or imidazolyl,

or Ra is hydrogen, Rb is C1-C8-alkyl substituted by imidazolyl, R3 is R6, and R4 is fluoro,

or Ra is hydrogen, Rb is C1-C8-alkyl substituted by benzoimidazolyl, R3 is R6, and R4 is fluoro,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by isoxazolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by pyrrolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

WO 2005/021519 PCT/EP2004/009586

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by pyrazolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by -CO-O-CH<sub>3</sub>, -CO-O-butyl, -CO-di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino, -CO-NH<sub>2</sub>, -NH-CO-C<sub>1</sub>-C<sub>8</sub>-alkyl, -SO<sub>2</sub>-C<sub>1</sub>-C<sub>8</sub>-alkyl, -CO-NH-R<sup>c</sup> where R<sup>c</sup> is napthyl, or by -CO-NH-C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or  $R^a$  is hydrogen,  $R^b$  is -CH(CH<sub>3</sub>)-CO-NH-C<sub>1</sub>-C<sub>8</sub>-alkyl or -CH(CH<sub>3</sub>)-CO-O-C<sub>1</sub>-C<sub>8</sub>-alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by -CH(OH)-CH<sub>2</sub>-OH, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>, or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkoxy, or by -S-C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being substituted by oxo, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by a 5- or 6-membered heterocyclic ring having three or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, -C<sub>1</sub>-C<sub>8</sub>-alkyl-di(C<sub>1</sub>-C<sub>8</sub>-alkyl)amino, or by C<sub>3</sub>-C<sub>8</sub>-cycloalkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by oxazolyl substituted by C<sub>3</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by imidazolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by hydroxy or C<sub>1</sub>-C<sub>8</sub>-alkoxy, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by -CO-Het where Het is a 5- or 6-membered heterocyclic ring having two or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being substituted by oxo, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or  $R^a$  is hydrogen,  $R^b$  is an aza-bicyclo[3.2.1]oct-3-yl ring optionally substituted by  $C_1$ - $C_8$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> and R<sup>b</sup> together form an azetidine ring substituted by C<sub>1</sub>-C<sub>8</sub>-alkoxycarbonyl or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> and R<sup>b</sup> together form a pyrrolidine ring substituted by -CO-NH<sub>2</sub> or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or Ra and Rb together form an imidazo-pyridine ring, R3 is R6, and R4 is R7;

R<sup>2</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl or halogen;

R<sup>5</sup> is hydrogen;

R<sup>6</sup> is halo or -SO<sub>2</sub>-CH<sub>3</sub>; and

R7 is hydrogen, halo, -SO<sub>2</sub>-CH<sub>3</sub>, nitrile, C<sub>1</sub>-C<sub>8</sub>-haloalkyl or imidazolyl.

### 3. A compound according to claim 1 or 2, wherein

Ra is hydrogen, Rb is C1-C4-alkyl substituted by pyridyl, R3 is R6, and R4 is fluoro or C1-C4-haloalkyl,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by hydroxy or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-haloalkyl,

or Ra is hydrogen, Rb is C1-C4-alkyl substituted by nitrile, R3 is fluoro, and R4 is R7,

or Ra is hydrogen, Rb is C1-C4-alkyl substituted by hydroxy, R3 is fluoro, and R4 is R7,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by di(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is C<sub>1</sub>-C<sub>4</sub>-haloalkyl,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_4$ -alkyl substituted by -O- $C_1$ - $C_4$ -alkyl-OH ,  $R^3$  is  $R^6$ , and  $R^4$  is fluoro or  $C_1$ - $C_4$ -haloalkyl,

or Ro is hydrogen, Rb is -CH(CH3)-CH2-OH, R3 is R6, and R4 is fluoro,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by pyrrolidinyl substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is C<sub>1</sub>-C<sub>4</sub>-haloalkyl,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by oxazolyl substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is nitrile or imidazolyl,

or Ra is hydrogen, Rb is C1-C4-alkyl substituted by imidazolyl, R3 is R6, and R4 is fluoro,

or Ra is hydrogen, Rb is C1-C4-alkyl substituted by benzoimidazolyl, R3 is R6, and R4 is fluoro,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_4$ -alkyl substituted by isoxazolyl substituted by  $C_1$ - $C_4$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_4$ -alkyl substituted by pyrrolyl substituted by  $C_1$ - $C_4$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by pyrazolyl substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by -CO-O-CH<sub>3</sub>, -CO-O-butyl, -CO-di(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, -CO-NH<sub>2</sub>, -NH-CO-C<sub>1</sub>-C<sub>4</sub>-alkyl, -SO<sub>2</sub>-C<sub>1</sub>-C<sub>4</sub>-alkyl, -CO-NH-R<sup>c</sup> where R<sup>c</sup> is napthyl, or by -CO-NH-C<sub>1</sub>-C<sub>4</sub>-alkyl optionally substituted by di(C<sub>1</sub>-C<sub>4</sub>-alkyl)amino, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or Ra is hydrogen, Rb is -CH(CH3)-CO-NH-C1-C4-alkyl or -CH(CH3)-CO-O-C1-C4-alkyl, R3 is R6, and R4 is R7,

or Ra is hydrogen, Rb is C1-C4-alkyl substituted by -CH(OH)-CH2-OH, R3 is R6, and R4 is R7,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkoxy, or by -S-C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being substituted by oxo, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by a 5- or 6-membered heterocyclic ring having three or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl, -C<sub>1</sub>-C<sub>8</sub>-alkyl-di(C<sub>1</sub>-C<sub>4</sub>-alkyl)-amino, or by C<sub>3</sub>-C<sub>5</sub>-cycloalkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or  $R^a$  is hydrogen,  $R^b$  is  $C_1$ - $C_4$ -alkyl substituted by oxazolyl substituted by  $C_3$ - $C_5$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by imidazolyl substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl optionally substituted by hydroxy or C<sub>1</sub>-C<sub>4</sub>-alkoxy, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl substituted by -CO-Het where Het is a 5- or 6-membered heterocyclic ring having two or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being optionally substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> is hydrogen, R<sup>b</sup> is a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, that ring being substituted by oxo, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or  $R^a$  is hydrogen,  $R^b$  is an aza-bicyclo[3.2.1]oct-3-yl ring optionally substituted by  $C_1$ - $C_4$ -alkyl,  $R^3$  is  $R^6$ , and  $R^4$  is  $R^7$ ,

or R<sup>a</sup> and R<sup>b</sup> together form an azetidine ring substituted by C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or R<sup>a</sup> and R<sup>b</sup> together form a pyrrolidine ring substituted by -CO-NH<sub>2</sub> or nitrile, R<sup>3</sup> is R<sup>6</sup>, and R<sup>4</sup> is R<sup>7</sup>,

or Ra and Rb together form an imidazo-pyridine ring, R3 is R6, and R4 is R7;

R<sup>2</sup> is C<sub>1</sub>-C<sub>4</sub>-alkyl or halogen;

R<sup>5</sup> is hydrogen;

R6 is halo or -SO2-CH3; and

R7 is hydrogen, halo, -SO2-CH3, nitrile, C1-C4-haloalkyl or imidazolyl.

## 4. A compound of formula I that is also a compound of formula XIII

where  $R^3$ ,  $R^4$  and  $R^6$  are as shown in the following table:

R³	R <sup>4</sup>	Rb
-SO₂CH₃	· F	
		, n
-SO₂CH₃	F	O_CH <sub>3</sub>
-SO₂CH₃	F	O CH <sub>3</sub>
-SO₂CH₃	F	
-SO <sub>2</sub> CH₃	F	
-SO₂CH₃	F	S_CH <sub>3</sub>
-SO₂CH₃	F	ОМОН
-SO₂CH₃	F	CH <sub>3</sub>
-SO <sub>2</sub> CH₃	F	H <sub>3</sub> C

R³	R <sup>4</sup>	Rb
-SO <sub>2</sub> CH <sub>3</sub>	F	
		NH NH
1		
-SO₂CH₃	F	i γ γ γ γ γ γ γ γ γ γ γ γ γ γ γ γ γ γ γ
302013	1	
		O CH <sub>3</sub>
-SO₂CH₃	F	CH <sub>3</sub>
302013	1	O CH <sub>3</sub>
50.077		VO VO 13
-SO <sub>2</sub> CH <sub>3</sub>	F	H₃C OU
		CH <sub>3</sub>
	1	O CH <sub>3</sub>
-SO₂CH₃	F	
		CH <sub>3</sub>
		N-N
-SO <sub>2</sub> CH <sub>3</sub>	F	, CH3
-3O <sub>2</sub> CF13	F	H
	<u> </u>	H3CIIII CH3
-SO₂CH₃	, F	l n
-SO <sub>2</sub> CH₃	F	
		H³C <sub>IIII</sub>
		он
-SO₂CH₃	F	ÇH₃
-SO₂CH₃	F	CH <sub>3</sub>
·		\ \N\
		CH <sub>3</sub>
-SO-CH	F	Ö
-SO <sub>2</sub> CH₃	r	CH₃ U
		N_CH₃
	,	
		استبرتنست سيست

R <sup>3</sup>	R <sup>4</sup>	R <sup>b</sup>
-SO <sub>2</sub> CH₃	F	O CH <sub>3</sub>
-SO₂CH₃	F	H <sub>3</sub> C NH <sub>2</sub>
-SO₂CH₃	F	NH <sub>2</sub>
-SO₂CH₃	F	CH <sub>3</sub> H <sub>3</sub> C CH <sub>3</sub>
-SO₂CH₃	-CF <sub>3</sub>	N N
-SO₂CH₃	-CF₃	NH CH <sub>3</sub>
-SO₂CH₃	-CF₃	N
-SO₂CH₃	-CF <sub>3</sub>	O_CH <sub>3</sub>
-SO <sub>2</sub> CH <sub>3</sub>	-CF <sub>3</sub>	ОН
-SO₂CH₃	-CF <sub>3</sub>	ОН
-SO₂CH₃	-CF₃	O CH <sub>3</sub>
-SO <sub>2</sub> CH <sub>3</sub>	-CF₃	
-SO₂CH₃	-CF₃	CH <sub>3</sub>

R <sup>3</sup>	R <sup>4</sup>	R <sup>b</sup>
-SO₂CH₃	-CF <sub>3</sub>	S_CH3
-SO₂CH₃	-CF₃	
-SO₂CH₃	-CF₃	CH <sub>3</sub>
-SO₂CH₃	-CF <sub>3</sub>	OH
-SO <sub>2</sub> CH₃	-CF <sub>3</sub>	H <sub>3</sub> C N
-SO₂CH₃	-CF <sub>3</sub>	
-SO₂CH₃	-CF <sub>3</sub>	O CH <sub>3</sub> CH <sub>3</sub>
-SO₂CH₃	-CF <sub>3</sub>	O_CH <sub>3</sub>
-SO <sub>2</sub> CH₃	-CF <sub>3</sub>	CEN
-SO₂CH₃	-CF <sub>3</sub>	N, CH3
-SO₂CH₃	-CF₃	П СН3
-SO₂CH₃	-CF <sub>3</sub>	H <sub>3</sub> C CH <sub>3</sub>
-SO₂CH₃	-CF <sub>3</sub>	н,с" Сн,

R <sup>3</sup>	R <sup>4</sup>	R <sup>b</sup>
-SO <sub>2</sub> CH <sub>3</sub>	-CF <sub>3</sub>	O CH <sub>3</sub> CH <sub>3</sub>
-SO₂CH₃	-CF₃	N CH <sub>3</sub>
-SO₂CH₃	·-CF <sub>3</sub>	н₃с" Н сн₃
-SO₂CH₃	-CF <sub>3</sub>	H <sub>3</sub> C,,OCH <sup>3</sup>
-SO₂CH₃	H	H³C
-SO₂CH₃	H	
-SO₂CH₃	н	O CH <sub>3</sub> CH <sub>3</sub>
-SO <sub>2</sub> CH <sub>3</sub>	Н	ОН
-SO₂CH₃	Н	ОН
-SO₂CH₃	Н	ОН
-SO₂CH₃	H	CH <sub>3</sub>
-SO₂CH₃	H	NH NH

R <sup>3</sup>	R <sup>4</sup>	R <sup>b</sup>
-SO₂CH₃	Н	O CH <sub>3</sub> CH <sub>3</sub>
-SO₂CH₃	Н	CIIN CIIN
-SO₂CH₃	CN	O CH <sub>3</sub> CH <sub>3</sub>
-SO₂CH₃	CN	CH <sub>3</sub>
-SO₂CH₃	CN	CH <sub>3</sub>
F	-SO₂CH₃	CEN
F	-SO₂CH₃	NH <sub>2</sub>
F	-SO₂CH₃	O II O CH <sub>3</sub>
F .	-SO <sub>2</sub> CH₃	O CH <sub>3</sub> CH <sub>3</sub>
· F	-SO <sub>2</sub> CH <sub>3</sub>	ОН
F	-SO₂CH₃	
F	-SO₂CH₃	
-SO₂CH₃	CI	H <sub>3</sub> C CH <sub>3</sub>

R <sup>3</sup>	R <sup>4</sup>	R <sup>b</sup>
-SO <sub>2</sub> CH <sub>3</sub>	F	OH

5. A compound of formula I that is also a compound of formula XIV

where R<sup>4</sup> and -NR<sup>a</sup>R<sup>b</sup> are as shown in the following table:

R <sup>4</sup> .	R*
F	R <sup>b</sup>
F	N N
F	N CH <sub>3</sub>
F	N N
н	O NH <sub>2</sub>
-CF <sub>3</sub>	NH <sub>2</sub>

R <sup>4</sup>	N R <sup>b</sup>
-CF <sub>3</sub>	NE CONTRACTOR OF THE PROPERTY
	N NH <sub>2</sub>

6. A compound of formula I that is also a compound of formula XV

where  $R^4$  and -Het are as shown in the following table:

R <sup>4</sup>	-Het
F	
F	н <sub>з</sub> с — сн <sub>з</sub>
F	0-N CH3
F	O-N CH <sub>3</sub>
F	O-N CH,
F	
F	O-N CH <sub>3</sub>
<b>F</b>	N-CH <sub>3</sub>

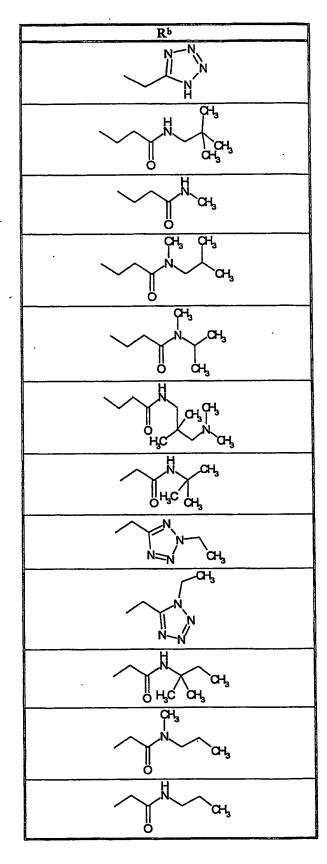
R <sup>4</sup>	-Het
F	S N CH <sub>3</sub>
F	CH <sub>3</sub>
F .	CH <sub>3</sub>
F	N N CH <sub>3</sub>
F	
F	
F	H <sub>3</sub> C CH <sub>3</sub>
F	T'A '
F	CH,
F	CH <sub>3</sub>
F	LN CH3
F	H <sub>3</sub> C CH <sub>3</sub>
F	LN CH3

R <sup>4</sup>	-Het
F	N.
	CH <sub>3</sub>
	сн
F	VN,
	0-CH <sub>3</sub>
F	N,
	OH
F	
	√ОН
	ÇH <sub>3</sub>
F	N.
F	CH <sub>3</sub>
F	
	T
	N CH <sub>3</sub>
F	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\
	L CH,
F	N. CH <sub>3</sub>
	N H <sub>3</sub> C CH <sub>3</sub>
	<u> </u>
F	
F	. \N.
	HN-N'N
F	N N
	H <sub>3</sub> C N-N
<u> </u>	
F	2,2
	N-N
	CH <sub>3</sub>
-CF <sub>3</sub>	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\
	CH <sub>3</sub>
Cl	N CH <sub>3</sub>
Cl	, N
	CH,
L	V1/3

R <sup>4</sup>	-Het
-CN	СН
-CN	O H <sub>3</sub> C CH <sub>3</sub>
	CH <sub>3</sub>
	CH <sub>3</sub>
	CH3
-CN	CH <sub>3</sub>
Н	LN CH3

# 7. A compound of formula I that is also a compound of formula XVI

where Rb is as shown in the following table:



R <sup>b</sup>
αH <sub>3</sub>
O OH,
CH <sub>3</sub> H <sub>3</sub> N <sub>4</sub> CH <sub>3</sub>
l b dy
CH <sub>3</sub>
O GH,
CH <sub>3</sub>
N-N CH3
O OH3
H <sub>H,C</sub> OH <sub>3</sub> OH <sub>3</sub>
N ari
વનુ વનુ
O CH <sub>3</sub>
विस्
h at
D H <sub>3</sub> C OH <sub>3</sub> OH <sub>3</sub>
A A of

- 8. A compound according to any one of claims 1 to 7 in combination with an anti-inflammatory, bronchodilatory, antihistamine or anti-tussive drug substance.
- 9. A compound according to any one of claims 1 to 7 for use as a pharmaceutical.

- 10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 7.
- 11. The use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for the treatment of a disease mediated by phosphatidylinositol 3-kinase.
- 12. The use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for the treatment of respiratory diseases, allergies, rheumatoid arthritis, osteoarthritis, rheumatic disorders, psoriasis, ulcerative colitis, Crohn's disease, septic shock, proliferative disorders such as cancer, atherosclerosis, allograft rejection following transplantation, diabetes, stroke, obesity or restenosis.
- 13. A process for the preparation of a compound of formula I as defined in claim 1, in free or salt form which comprises the steps of:
- (i) (A) reacting a compound of formula II

$$\mathbb{R}^3$$
 $\mathbb{R}^4$ 
 $\mathbb{R}^2$ 
 $\mathbb{R}^3$ 
 $\mathbb{R}^4$ 

wherein R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as claimed in claim 1 and T is a 5- or 6-membered heterocyclic ring having one or more ring hetero atoms selected from the group consisting of oxygen, nitrogen and sulphur, with a compound of formula III

wherein R<sup>a</sup> and R<sup>b</sup> are as claimed in claim 1;

(B) reacting compounds of formula IV

wherein  $R^2$ ,  $R^3$ ,  $R^4$  and  $R^5$  are as claimed in claim 1 with a compound of formula III wherein  $R^a$  and  $R^b$  are as claimed in claim 1;

WO 2005/021519 PCT/EP2004/009586

(C) for the preparation of compounds of formula I where R<sup>a</sup> is hydrogen and R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>b</sup> are as claimed in claim 1, reacting a compound of formula V

$$R^{5}$$
 $N$ 
 $NH_{2}$ 
 $R^{3}$ 
 $R^{4}$ 

wherein R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as claimed in claim 1, with a compound of formula VI

$$R^b - N = C = O$$
 VI

wherein Rb is as claimed in claim 1; or

(D) for the preparation of compounds of formula I where R<sup>a</sup> is hydrogen, R<sup>b</sup> is C<sub>1</sub>-C<sub>8</sub>-alkyl substituted by imidazolyl substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl optionally substituted by hydroxy or C<sub>1</sub>-C<sub>8</sub>-alkoxy and R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as claimed in claim 1, reacting a compound of formula V where R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are as claimed in claim 1, with a compound of formula VII

where Q is C1-C8-alkyl optionally substituted by hydroxy or C1-C8-alkoxy; and

(ii) recovering the resultant compound of formula I in free or salt form.